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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,321	05/22/2007	Robert D. Hill	049280-0102	4952

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EXAMINER	
WORLEY, CATHY KINGDON	
ART UNIT	PAPER NUMBER
1638	

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03/10/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,321	HILL ET AL.	
	Examiner	Art Unit	
	CATHY K. WORLEY	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-32* is/are pending in the application.

4a) Of the above claim(s) *25-27,29 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,28, 30, and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *BLAST_Sowa; BLAST_alfalfa*.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :6/9/06; 6/10/08; 12/10/08; 10/22/09; 11/30/09; and 2/4/11.

DETAILED ACTION

Restriction/Election

1. In response to the communication received on Feb. 4, 2011, from Courtenay C. Brinckerhoff, the election with traverse of group II, claims 24, 28, and 30-32 as they related to a decrease in level of expression of non-symbiotic hemoglobin, is acknowledged.

The Applicant traverses on the grounds that no lack of unity was found in the PCT application or the EP application (see second paragraph on page 5 of the response filed on Feb. 4, 2011). This is not persuasive, however, because the USPTO makes its own determination independent from the determination of other Patent Offices and independent of the determination of the International Search Authority.

The Applicant argues that the Examiner did not show a serious examination burden such as separate classification, separate status in the art or separate field of search (see third paragraph on page 5). This is not persuasive, however, because inhibition of expression is completely different than overexpression and has completely different issues under 35 USC 112, therefore, there would be a burden to consider both inventions. Furthermore, there is no requirement for the examiner to

address different classification, status in the art, or field of search for establishing lack of unity.

The Applicant argues that the technical feature linking the inventions is a method of modifying a plant phenotype of a plant grown under normal oxygen conditions (see paragraph bridging pages 5-6 of the response). This is not persuasive, however, because the modified phenotype of plants in which expression has been decreased is different than the modified phenotype of plants in which expression is increased, therefore, the two inventions do not share the same phenotype.

The Applicant argues that the requirement should be an election of species rather than a restriction between inventions (see second paragraph on page 6 of the response). This is not persuasive, however, because the two inventions do not share a common function, therefore, they are not species of a generic invention that share a common function.

The restriction requirement based on lack of unity is proper and is MADE **FINAL**.

Claims 24-32 are pending in the instant application, claims 25-27, 29, and 31 are withdrawn from consideration for being directed to non-elected inventions. The Applicant is reminded to amend claim 24 to delete references to an increase in expression and recite only the elected invention of a **decrease** in expression. Claims 24, 28, 30, and 32 are examined in this Office Action.

Application Data Sheet

2. The Application Data Sheet (ADS) provided on April 18, 2007, is objected to because it continues to include reference to PCT/IB2004/004119, which is a typographical error. The Applicant is advised to provide a corrected ADS that refers only to PCT/IB2004/004419.

Claim Objections

3. Claim 24 is objected to because of the following: the claim continues to recite the non-elected embodiment of an increased level of expression of non-symbiotic hemoglobin. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 24, 28, 30, and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly

claim the subject matter which applicant regards as the invention. All dependent claims are included in these rejections.

The term "normal oxygen conditions" in claim 24 is a relative term which renders the claim indefinite. The term "normal oxygen conditions" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The instant specification states that "a transient hypoxic phase may be experienced during germination" (see lines 13-15 on page 4). This implies that hypoxic phases can be part of the normal germination process. It is unclear if "normal oxygen conditions" excludes a hypoxic phase during germination. Furthermore, it is unclear what range of oxygen conditions is considered "normal". The metes and bounds of "normal oxygen conditions" has not been defined. For these reasons, no weight is given to "normal oxygen conditions" for the purpose of examination.

5. Claims 24, 28, 30, and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are broadly drawn to a method of modifying a plant phenotype by transforming a plant with an expression vector comprising a nucleotide sequence encoding a plant non-symbiotic hemoglobin or an antisense sequence thereto, thereby yielding a transformed plant having an altered level of expression of non-symbiotic plant hemoglobin as compared to a non-transformed control plant (applicant elected a DECREASE in expression level); wherein said transformed plant exhibits, under normal oxygen conditions, a plant phenotype that is modified as compared to said non-transformed control plant, wherein said phenotype is selected from the group consisting of shoot or root apical dominance; flower color; and chlorophyll content.

Applicants teach transgenic alfalfa plants transformed with antisense constructs comprising a barley non-symbiotic hemoglobin (see last two paragraphs

on page 13). The specification refers to Dordas et al (2003) for information about the constructs. Dordas et al refer to Sowa et al (1998) (see "Experimental procedures" "Construction of transformation vectors" in left column of page 768 of Dordas et al). Neither the specification, nor Dordas et al, nor Sowa et al identify the particular cDNA that was utilized in the constructs, other than calling it a barley non-symbiotic hemoglobin.

The Applicants teach that two antisense lines of alfalfa were generated, referred to as Hb-(4) and Hb-(44). These lines has lower hemoglobin content compared to the control (see Table 1 on page 15). The intensity of the purple color of the flowers increased as the nsHb expression declined (see lines 25-27 on page 17). The taproot diameter was decreased relative to the control plants (see Figure 5). The total chlorophyll content was diminished for the antisense lines (see paragraph bridging pages 17-18 of the specification). The antisense plants had a reduction in mean internode length and areas per leaflet (see lines 11-12 on page 20). The antisense plants had greater numbers of stems per plant, nodes per stem, and leaflets per plant (see lines 15-16 on page 20). The antisense plants had compressed oval leaflets with shortened petioles and petiolules (see lines 20-21 on page 20). The antisense plants had altered nutrient concentration in the shoots 35 days after transplanting (see Table 4 on page 23).

Applicants do not teach the identity of the barley cDNA utilized for their antisense constructs. The Applicants do not teach any transgenic plants other than

transgenic alfalfa, and they do not teach any antisense constructs other than the ones utilized by Dordas et al and Howa et al that contain a barley non-symbiotic hemoglobin. The reference by Dordas et al was not incorporated by reference, therefore, even if it did disclose a particular cDNA, it could not be relied upon to provide enablement.

The state-of-the-art is such that one of skill in the art cannot predict the tissue-specificity or function of non-symbiotic hemoglobins. See, for example, Arrendondo-Peter et al (Plant Physiol. (1998) Vol. 118; pp. 1121-1125) who teach that non-symbiotic hemoglobins have potentially differing biochemical properties and have expression patterns in plant tissues that vary significantly (see right column on page 1122). Some non-symbiotic hemoglobins are expressed in root meristems and vasculature, whereas others are expressed in rosette leaves, and others in leaves and roots (see right column on page 1122). Some are induced by low temperature, some by hypoxic conditions, some may be regulated by calcium-dependent protein kinases (see right column on page 1122). They teach that non-symbiotic hemoglobins could have several functions in situ (see first paragraph on page 1124). For these reasons, the phenotype that results from the inhibition of expression of a hemoglobin in alfalfa can not be relied upon to predict the phenotype that might result from inhibition of expression of other non-symbiotic hemoglobins in other plant species.

Antisense suppression of gene expression is highly unpredictable, especially for members of a multi-gene family such as the hemoglobin gene family, and the prior art suggests that success depends on the percent identity between the sequence of the antisense construct and the target gene sequence (see Elomaa et al (1996) Molecular Breeding, Vol. 2, pp. 41-50; paragraph bridging pages 47-48, in particular). In another study, Colliver et al taught that antisense of members of a gene family is highly unpredictable (PMB (1997) Vol. 35, pp. 509-522). Colliver et al showed that transformation of bird's foot trefoil with a construct that was antisense to bean chalcone synthase resulted in transformants with increased levels of chalcone synthase transcripts due to increased transcription of other members of the gene family (see page 519, left column, paragraph 2). Because of the sequence variability between the different genes in different species of plants and because of the inconsistent results taught in the prior art, there is a high degree of unpredictability in the use of antisense to inhibit the expression of different genes.

Furthermore, the instant specification does not provide enough information about the identity of the barley hemoglobin that was utilized in the experiments. The Examiner attempted to identify the barley cDNA by following the reference trail (Dordas et al was cited in the specification, and Dordas et al cited Howa et al), however, these references do not identify the barley gene. The Examiner searched in GenBank and found a barley hemoglobin cDNA that included Sowa as an author; the accession is U94968. The Examiner then performed a BLAST search to

determine which genes in alfalfa would have sufficient identity to be candidates for inhibition of expression upon introduction of an antisense construct that was made with the barley cDNA. The BLAST search identified homologous genes in wheat, corn, rice, and sugar cane; but no homologous genes were found in alfalfa (see BLAST results provided with this Office Action).

Next, the Examiner searched in GenBank for alfalfa non-symbiotic hemoglobins and found accession AF172172.1. The Examiner performed a BLAST search with this alfalfa cDNA (see BLAST results provided with this Office Action). There were no barley genes identified.

Next the Examiner did a one-on-one alignment of the barley cDNA and the alfalfa cDNA. The results are included, below:

Title: AF172172
Perfect score: 483
Sequence: 1 ATGGGCACTTTGGATACAAA.....AAATGAAACCTTCCTCTTAG 483

Scoring table: IDENTITY_NUC
Gapop 10.0 , Gapext 0.5

Searched: 1 seqs, 1173 residues

Total number of hits satisfying chosen parameters: 2

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : hvu94968.gb_pln:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	55	11.4	1173	1	HVU94968	ACCESSION:U94968
c 2	21.4	4.4	1173	1	HVU94968	ACCESSION:U94968

ALIGNMENTS

RESULT 1
HVU94968
LOCUS HVU94968 1173 bp DNA linear PLN 15-SEP-1997
DEFINITION Hordeum vulgare hemoglobin gene, complete cds.
ACCESSION U94968
VERSION U94968.1 GI:2071975
KEYWORDS .
SOURCE Hordeum vulgare

```
  ORGANISM  Hordeum vulgare
            Eukaryota; Viridiplantae; Streptophyta; Embryophyta; Tracheophyta;
            Spermatophyta; Magnoliophyta; Liliopsida; Poales; Poaceae; BEP
            clade; Pooideae; Triticeae; Hordeum.
REFERENCE   1  (bases 1 to 1173)
  AUTHORS   Guy,P.A., Sowa,A. and Hill,R.D.
  TITLE     The electronic Plant Gene Register
  JOURNAL   Plant Physiol. 114 (3), 1135-1136 (1997)
   PUBMED   9289746
REFERENCE   2  (bases 1 to 1173)
  AUTHORS   Guy,P.A., Sowa,A.W. and Hill,R.D.
  TITLE     Direct Submission
  JOURNAL   Submitted (21-MAR-1997) Plant Science, University of Manitoba,
            University Crescent, Winnipeg, MB R3T 2N2, Canada
FEATURES             Location/Qualifiers
     source          1. .1173
                     /organism="Hordeum vulgare"
                     /mol_type="genomic DNA"
                     /db_xref="taxon:4513"
     mRNA            join(<1. .144,242. .356,456. .572,695. .>1173)
                     /product="hemoglobin"
     5'UTR           <1. .28
     CDS             join(29. .144,242. .356,456. .572,695. .835)
                     /note="mRNA sequence deposited under GenBank Accession
                     Number U01228"
                     /codon_start=1
                     /product="hemoglobin"
                     /protein_id="AAB70097.1"
                     /db_xref="GI:2071976"
                     /translation="MSAAEGAVVFSEEKEALVLKSWAIMKKDSANLGLRFFLKIFEIA
                     PSARQMFPFLRDSDVPLETNPKLKTHAVSVFVMTCEAAAQLRKAGKITVRETTLKRLG
                     GTHLKYGVADGHFEVTRFALLETIKEALPADMWGPEMRNAWGEAYDQLVAAIKQEMKP
                     AE"
     3'UTR           836. .>1173

  Query Match             11.4%;  Score 55;  DB 1;  Length 1173;
  Best Local Similarity   64.6%;  Pred. No. 0;
  Matches   82;  Conservative    0;  Mismatches   45;  Indels    0;  Gaps    0;

Qy        102 GCTTTTCTTGAAAATATTTGAGATTGCTCCATCAGCTCAAAAACTTTTCTCATTCTTGAA 161
              || |  ||  |  || || ||||| || || || ||     |  | ||| | ||| ||
Db        230 GCGTGCCTCCAGGATCTTCGAGATCGCGCCGTCGGCGAGGCAGATGTTCCCGTTCCTGCG 289

Qy        162 AGATTCAAAAGTTCCTTTGGAGCAAAACACCAAGCTCAAGCCTCATGCCATGTCTGTCTT 221
               || ||  | || ||  |||||   ||| ||||||||||| | || ||| |||| |||||
Db        290 CGACTCCGACGTGCCGCTGGAGACCAACCCCAAGCTCAAGACCCACGCCGTGTCCGTCTT 349

Qy        222 TCTCATG 228
                |||||
Db        350 CGTCATG 356
```

These results demonstrate that there is not sufficient homology between this particular barley cDNA and this particular alfalfa cDNA for an antisense construct comprising one to inhibit expression of the other. For this reason, the Examiner does not know which barley cDNA was utilized in the working examples in the instant application, and the Examiner does not know which alfalfa gene was inhibited. Therefore the instant application is not enabling for reproducing the working examples that are set forth.

The Applicant is invited to deposit seeds from the two antisense alfalfa lines and bring the application in compliance with 37 CFR 1.801-1.809. If the Applicant provides the necessary biological deposit, then the instant application would be enabling for the two particular alfalfa plants that are described in the working examples (Hb-(4) and Hb-(44)).

Even if a biological deposit were relied upon to provide enablement for these two alfalfa plants, the enablement would not be extended to other plants because one of skill in the art would not know how to make the antisense constructs.

Even if one of skill in the art could identify the barley cDNA to be able to make the constructs, there is a high degree of unpredictability about what phenotype would results in any plant other than alfalfa. Would other plant species also have darker purple flowers, less chlorophyll, a reduction in mean internode length and areas per leaflet, greater numbers of stems per plant, nodes per stem, and leaflets per plant, compressed oval leaflets with shortened petioles and

petiolules, and altered nutrient concentration in the shoots? Would they have these phenotypes even if the homologous endogenous gene is only expressed in roots? Or if the homologous endogenous gene is expressed in response to calcium or low temperature? Given this high degree of unpredictability for what phenotype would be expected upon inhibition of expression of any particular non-symbiotic hemoglobin gene family member, undue trial and error experimentation would be required for one of skill in the art to make multiple antisense constructs utilizing multiple non-symbiotic hemoglobin genes and transform multiple plant species with these constructs and screen for phenotypes.

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the method of the claimed invention, and therefore, the invention is not enabled.

6. Claims 24, 28, 30, and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method of modifying a plant phenotype by transforming a plant with an expression vector comprising a nucleotide sequence

encoding a plant non-symbiotic hemoglobin or an antisense sequence thereto, thereby yielding a transformed plant having an altered level of expression of non-symbiotic plant hemoglobin as compared to a non-transformed control plant (applicant elected a DECREASE in expression level); wherein said transformed plant exhibits, under normal oxygen conditions, a plant phenotype that is modified as compared to said non-transformed control plant, wherein said phenotype is selected from the group consisting of shoot or root apical dominance; flower color; and chlorophyll content.

Applicants describe transgenic alfalfa plants transformed with antisense constructs comprising a barley non-symbiotic hemoglobin (see last two paragraphs on page 13). The specification refers to Dordas et al (2003) for information about the constructs. Dordas et al refer to Sowa et al (1998) (see "Experimental procedures" "Construction of transformation vectors" in left column of page 768 of Dordas et al). Neither the specification, nor Dordas et al, nor Sowa et al identify the particular cDNA that was utilized in the constructs, other than calling it a barley non-symbiotic hemoglobin.

The Applicants describe two antisense lines of alfalfa that were generated and are referred to as Hb-(4) and Hb-(44). These lines have lower hemoglobin content compared to the control (see Table 1 on page 15). The intensity of the purple color of the flowers increased as the nsHb expression declined (see lines 25-27 on page 17). The taproot diameter was decreased relative to the control plants

(see Figure 5). The total chlorophyll content was diminished for the antisense lines (see paragraph bridging pages 17-18 of the specification). The antisense plants had a reduction in mean internode length and areas per leaflet (see lines 11-12 on page 20). The antisense plants had greater numbers of stems per plant, nodes per stem, and leaflets per plant (see lines 15-16 on page 20). The antisense plants had compressed oval leaflets with shortened petioles and petiolules (see lines 20-21 on page 20). The antisense plants had altered nutrient concentration in the shoots 35 days after transplanting (see Table 4 on page 23).

Applicants do not describe the identity of the barley cDNA utilized for their antisense constructs. The Applicants do not describe any transgenic plants other than transgenic alfalfa, and they do not describe any antisense constructs other than the ones utilized by Dordas et al and Howa et al that contain a barley non-symbiotic hemoglobin. The reference by Dordas et al was not incorporated by reference, therefore, even if it did disclose a particular cDNA, it could not be relied upon to provide written description.

The state-of-the-art is such that one of skill in the art cannot predict the tissue-specificity or function of non-symbiotic hemoglobins. See, for example, Arrendondo-Peter et al (Plant Physiol. (1998) Vol. 118; pp. 1121-1125) who teach that non-symbiotic hemoglobins have potentially differing biochemical properties and have expression patterns in plant tissues that vary significantly (see right column on page 1122). Some non-symbiotic hemoglobins are expressed in root

meristems and vasculature, whereas others are expressed in rosette leaves, and others in leaves and roots (see right column on page 1122). Some are induced by low temperature, some by hypoxic conditions, some may be regulated by calcium-dependent protein kinases (see right column on page 1122). They teach that non-symbiotic hemoglobins could have several functions in situ (see first paragraph on page 1124). For these reasons, the phenotype that results from the inhibition of expression of a hemoglobin in alfalfa can not be relied upon to predict the phenotype that might result from inhibition of expression of other non-symbiotic hemoglobins in other plant species.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F. 3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The Applicants fail to describe a representative number of antisense constructs effective for altering shoot or root apical dominance, flower color, or chlorophyll content. The Applicants only describe alfalfa lines Hb-(4) and Hb-(44) which have darker purple flowers, reduced chlorophyll content and altered root and

shoot morphology. Furthermore, the Applicants fail to describe structural features common to members of the claimed genus of antisense constructs effective for altering shoot or root apical dominance, flower color, or chlorophyll content. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for a non-symbiotic hemoglobin gene to be effective for antisense inhibition of an endogenous gene that will result in altering shoot or root apical dominance, flower color, or chlorophyll content, it remains unclear what features identify antisense constructs capable of such activity. Since the genus of antisense constructs effective for altering shoot or root apical dominance, flower color, or chlorophyll content has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Constructs comprising a sequence encoding a non-symbiotic hemoglobin encompass any member of the non-symbiotic hemoglobin gene family across the entire plant Kingdom, many of which would not alter shoot or root apical dominance, flower color, or chlorophyll content upon being expressed in a plant, and most of which were not in the possession of the Applicant at the time of filing. The Applicants have reduced to practice only one antisense construct in one species of plant that resulted in darker purple flower color, reduced chlorophyll content, and altered root and shoot morphology. Accordingly, the specification fails to provide an adequate written description to support the genus of antisense constructs effective

for altering shoot or root apical dominance, flower color, or chlorophyll content as set forth in the claims. (See Written Description guidelines published in 2008 online at http://www.uspto.gov/web/menu/written.pdf).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 24, 28, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dordas et al (The Plant Journal (2003) Vol. 35; pp. 763-770).

The claims are drawn to a method of modifying a plant phenotype by transforming a plant with an expression vector comprising a nucleotide sequence encoding a plant non-symbiotic hemoglobin or an antisense sequence thereto, thereby yielding a transformed plant having an altered level of expression of non-symbiotic plant hemoglobin as compared to a non-transformed control plant (applicant elected a DECREASE in expression level); wherein said transformed plant exhibits, under normal oxygen conditions, a plant phenotype that is modified as compared to said non-transformed control plant, wherein said phenotype is

selected from the group consisting of shoot or root apical dominance; flower color; and chlorophyll content.

Dordas et al teach transgenic alfalfa root cultures that are transformed with an antisense construct made from a barley non-symbiotic hemoglobin cDNA (see left column on page 768). These lines are referred to as "3" for the "sense" line, "C" for the control, and "44" for the antisense line (see Figure 7 on page 767), and these appear to be the same as the lines utilized in the instant application (see Figure 2 of the instant application). The amount of hemoglobin in the antisense lines was reduced (see Table 1 on page 764).

Dordas et al do not teach a whole plant that is transformed with the antisense construct. Dordas et al do not teach a phenotype for a whole plant.

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to regenerate a whole plant from the transgenic alfalfa roots taught by Dordas et al. One would have been motivated to generate a whole plant because this would allow studying the phenotype in tissues other than root tissues. It also would allow for long term storage of the germplasm in the form of dried seeds which is much more convenient, less labor intensive, and less costly compared to continuous tissue culture of root cultures. Regenerating a whole plant would also allow for making a homozygous line and performing genetic analyses. The phenotype of darker purple flowers, reduced chlorophyll, and altered

root and shoot morphology would naturally flow from the regeneration of the antisense line 44 taught by Dordas et al.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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